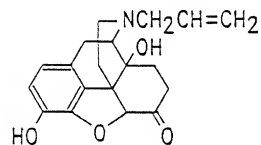
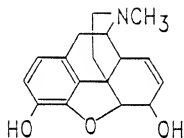
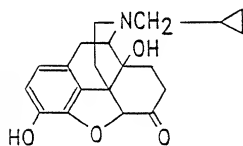


Morphine



Naloxone



Naltrexone (R=O)

Nalmefene (R=CH₂).

FIG. 1

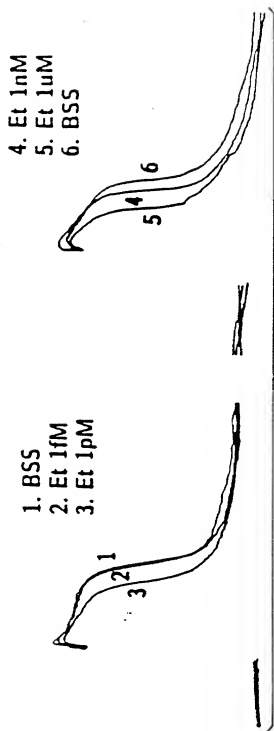


FIG. 2A

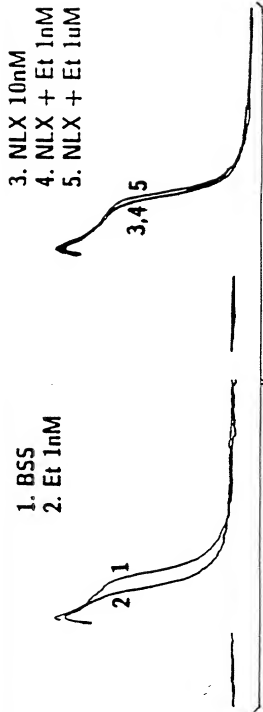


FIG. 2B

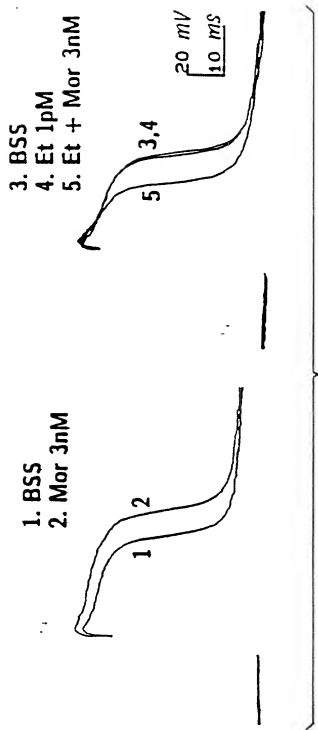


FIG. 2C

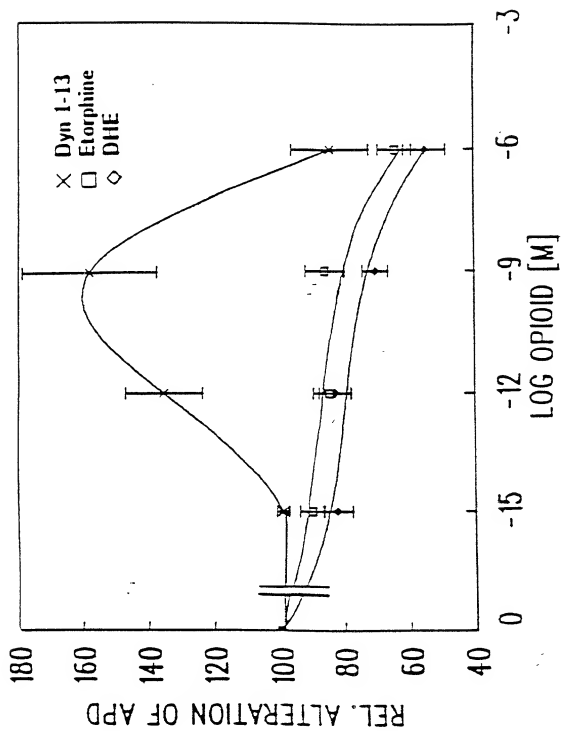


FIG. 3

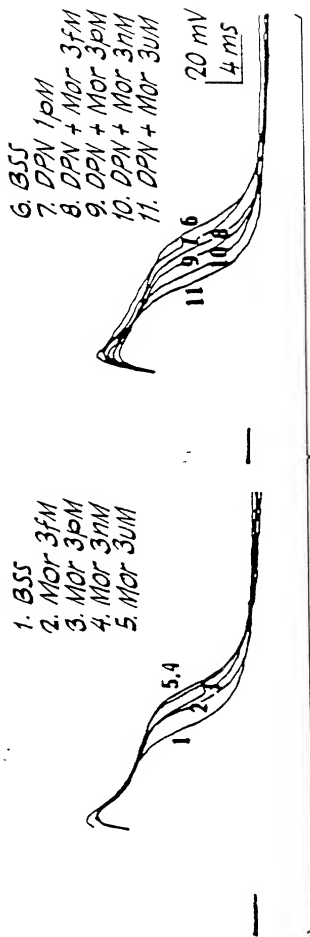


FIG. 4A

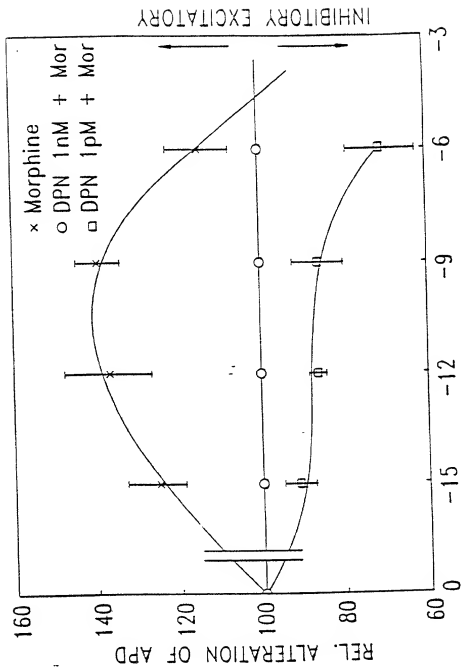


FIG. 4B.

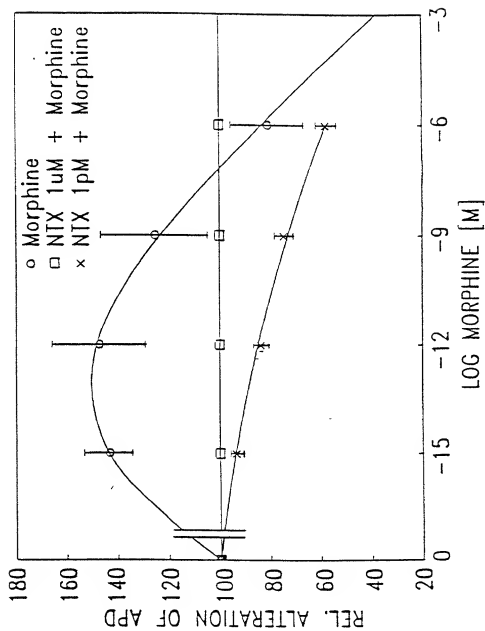


FIG. 5

Acute Test	Alteration of Action Potential Duration (APD)				
	(APD shortening: ↓ ; APD prolongation: ↑ ; No APD change: 0)		Chronic Morphine-Treated Neurons (1μM; >1wk)		
	Naive DRG Neurons	BSS + Antag. at Excit.Op.Rec. (pM)	Chronic Co-treatment with Mor + Antag. at Excit. Op. Rec. (pM)		
	Control BSS		After Washout with BSS		
1 - 10 μM morphine	↓ (inhibitory) ("analgesia")	↑↑	↓ ("tolerance")	↑	
pM - nM morphine	↑ ("excitatory analgesia")	↓ (unmasking of inhibitory effects)	↓	↑	
~ fM morphine or dyn A-(1-13)	0	0	↓ (excitatory supersensitivity)	0	
nM naloxone	0	0	↓ ("dependence") ("withdrawal effect")	0	

FIG. 6

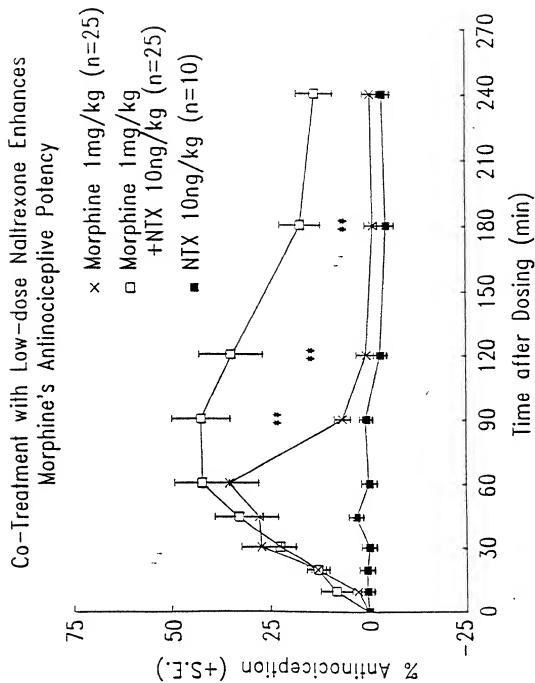


FIG. 7

Co-Treatment with Low-Dose Naltrexone Attenuates
Acute and Chronic Morphine Dependence

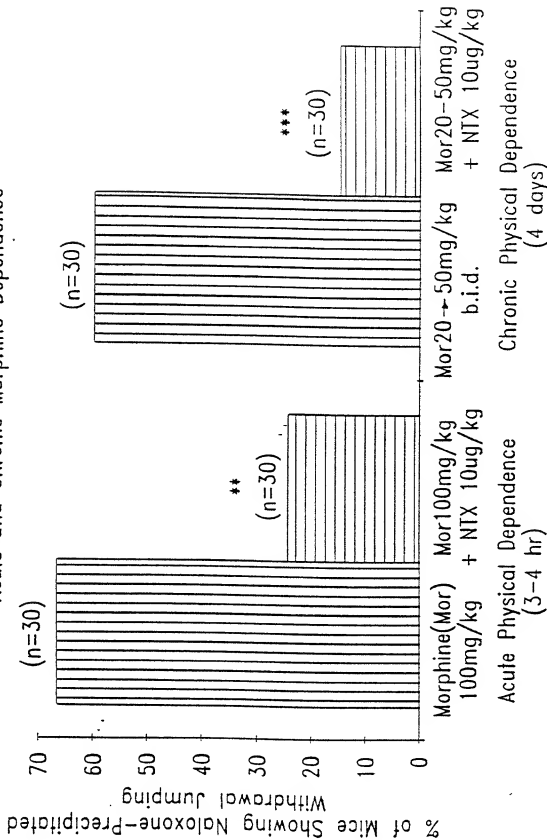


FIG. 8

Co-Treatment with Ultra-Low Dose Nalmefene Enhances
Morphine Antinociceptive Potency

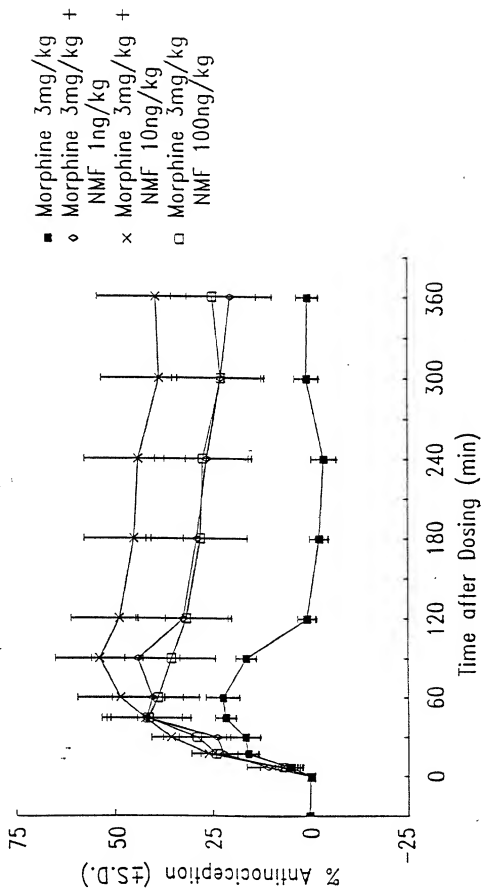


FIG. 9

Co-Treatment with Low-Dose Nallexone or Nalmefene
Attenuates Acute Morphine Dependence

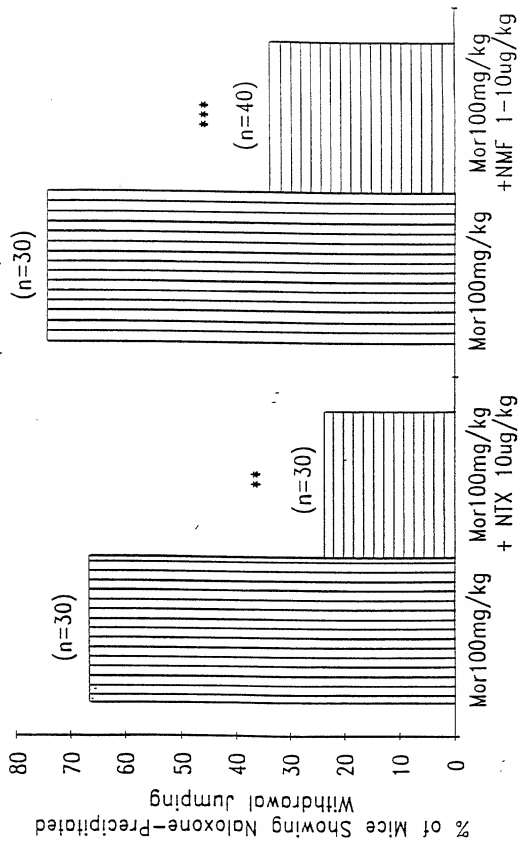


FIG. 10